

## SPECIAL ARTICLES

## Recommended protocols for the Multiple Sleep Latency Test and Maintenance of Wakefulness Test in adults: guidance from the American Academy of Sleep Medicine

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This article updates the American Academy of Sleep Medicine protocols for the administration of the Multiple Sleep Latency Test and the Maintenance of Wakefulness Test. The American Academy of Sleep Medicine commissioned a task force of clinical experts in sleep medicine to review published literature on the performance of these tests since the publication of the 2005 American Academy of Sleep Medicine practice parameter paper. Although no evidence-based changes to the protocols were warranted, the task force made several changes based on consensus. These changes included guidance on patient preparation, medication and substance use, sleep before testing, test scheduling, optimum test conditions, and documentation. This article provides guidance to providers who order and administer the Multiple Sleep Latency Test and the Maintenance of Wakefulness Test.

**Keywords:** Multiple Sleep Latency Test, Maintenance of Wakefulness Test, protocol, sleep testing

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### BACKGROUND

The assessment of sleepiness is an important part of the evaluation of patients with sleep disorders. The Multiple Sleep Latency Test (MSLT)<sup>1</sup> and the Maintenance of Wakefulness Test (MWT)<sup>2</sup> are objective measures of sleepiness and alertness, respectively. This article updates the American Academy of Sleep Medicine (AASM) standardized protocols for these tests in adults aged 18 years and older based on literature review and expert consensus. Normative data or clinical indications for the tests are not addressed in detail in this document but can be found in the 2005 AASM review paper.<sup>3</sup> The indications and diagnostic criteria for the disorders of central hypersomnolence utilizing the MSLT can be found in the most recent edition of the *International Classification of Sleep Disorders* (ICSD).<sup>4</sup>

Although the MSLT and MWT procedures are similar, there is a low correlation ( $r = .41$ ) between the tests, suggesting that they are measuring different properties.<sup>5</sup> The MSLT objectively measures sleep propensity in the absence of external alerting factors. A shorter sleep latency reflects greater daytime sleepiness. Several measurements of sleep latency at regular intervals across the day are averaged to calculate a mean sleep latency (MSL). The MSL and the number of naps in which rapid eye movement (REM) sleep occurs are criteria used for the diagnoses of narcolepsy type 1 and 2 and idiopathic hypersomnia.<sup>4</sup> The MSLT is also used to assess persistent sleepiness after the treatment of other sleep disorders such as obstructive sleep apnea (OSA). Accurate

measurement of physiological sleep tendency requires minimizing environmental and alerting factors.<sup>4</sup>

In contrast, the MWT measures the ability to stay awake. The MWT is a modification of the MSLT and is used to objectively measure the ability to stay awake under nonstimulating conditions for a defined period of time.<sup>3</sup> An increased ability to stay awake in the context of trying to remain awake is reflected in a prolonged sleep latency. Analogous to the MSLT, several measurements of sleep latency at regular intervals across the day are averaged to calculate the MSL. The MWT is used to evaluate response to treatment for conditions associated with excessive sleepiness and to assess alertness in individuals who must remain awake for safety reasons.<sup>3,6</sup>

### PROTOCOLS FOR MSLT

The protocol for the MSLT is presented in **Box 1** and **Box 2**.

### Considerations for the MSLT

The objective of the MSLT is to measure a patient's physiological tendency to fall asleep under standardized conditions. Several factors concerning patient preparation and test performance need to be considered to acquire reliable data during the MSLT. These considerations are discussed in detail herein and are intended to provide additional guidance in conducting the

**Box 1—MSLT clinical guidance and patient preparation.**

1. In preparation, the clinician and the patient should define goals for adequate sleep at home with regard to timing and duration. Adequate sleep should be documented by sleep diary and, when available, actigraphy for 2 weeks before testing.
2. In patients who are undergoing an MSLT for persistent sleepiness despite treatment of a sleep disorder such as OSA, the MSLT should be conducted when the patient is clinically stable and when treatments for existing sleep disorders are well-established and effective. For patients with sleep-disordered breathing treated with PAP therapy, the clinician should ensure efficacy and adherence based on a review of downloaded data. If the patient is using non-PAP therapy for sleep-disordered breathing, then self-report of adequate use and efficacy of therapy should be confirmed before the MSLT. If adequate effectiveness is suboptimal, then the clinician should determine if the anticipated impact on the test results warrant rescheduling. The patient should use PAP and/or non-PAP therapy during PSG on the night before the MSLT.
3. The clinician should develop a plan regarding use of prescription medication, OTC agents, herbal remedies, and other substances. In general, medications with alerting, sedating, and/or REM-sleep-modulating properties should be stopped at least 2 weeks before the MSLT. Clinical judgment should be used regarding changes to medications that could impair patient safety. The patient should be instructed to consult with the clinician before starting any prescription or OTC medication before the test.
4. The clinician should discuss acceptable caffeine consumption with the patient before testing to avoid confounding the MSLT results while avoiding caffeine withdrawal symptoms on the day of the test. The goal should be abstinence, and when necessary, withdrawal should be preceded by a taper.

MSLT = Multiple Sleep Latency Test, OSA = obstructive sleep apnea, OTC = over the counter, PAP = positive airway pressure, PSG = polysomnography, REM = rapid eye movement.

**Box 2—MSLT general testing, data acquisition, and reporting procedures.****General Testing Procedures**

1. The MSLT should be performed after an attended PSG, which allows a minimum 7 hours of time in bed with at least 6 hours of sleep, with timing that corresponds with the patient's major sleep period. The test should not be performed after a night during which PAP pressures were adjusted (split-night or PAP titration study).
2. The patient's clothing should be comfortable, be appropriate to the environment, and not interfere with the performance of tests. A change in clothing is not required between the PSG and MSLT.
3. The patient should abstain from alcohol, caffeine, marijuana, and other sedating or alerting agents on the day of the test. Nicotine use is discouraged but if unavoidable should be terminated at least 30 minutes before a nap trial.
4. Patients on PAP/non-PAP therapies for sleep-disordered breathing should use them during the PSG and MSLT. The PAP settings and mask interface should match those used at home.
5. The recording montage for the MSLT should, at a minimum, include 3 EEG recording leads with at least 1 each for frontal (F3-M2 or F4-M1), central (C3-M2 or C4-M1), and occipital (O1-M2 or O2-M1) derivations, left and right eye EOGs, mental/submental EMG, and EKG. Other recording devices or sensors used for the PSG are unnecessary and should be removed to promote patient comfort.
6. Audiovisual recordings must be made during the nap trials and be accessible to interpreting clinicians. The patient must be audiovisually monitored throughout the day, but retention of recordings made between nap trials is discretionary.
7. The MSLT should consist of 5 nap trials. The initial trial should begin 1.5–3 hours after termination of the nocturnal recording. Each subsequent trial should begin 2 hours after the start of the prior trial. Only when the results are clearly diagnostic of narcolepsy after 4 naps with mean latency  $\leq$  8 minutes and 2 or more SOREMPs have occurred (either because of 2 or more SOREMPs during the nap trials or 1 in the nap trials and 1 during the PSG) should a shorter 4-nap trial test be performed.
8. Before each nap trial, the patient should be offered the use of the restroom and queried regarding other requirements for comfort.
9. Sleep rooms should be dark, quiet, and at a comfortable temperature during testing.
10. The patient should be lying in bed for all nap trials.
11. Patient bio-calibrations should be conducted before starting each nap trial. Standard instructions include: (1) "lie quietly with your eyes open for 30 seconds"; (2) "close both eyes for 30 seconds"; (3) "without moving your head, look to the right, then left, then right, then left, right and then left"; (4) "blink eyes slowly for 5 times"; and (5) "clench or grit your teeth tightly together."
12. At the start of each nap trial, the patient should be instructed as follows: "Please lie quietly, assume a comfortable position, keep your eyes closed, and allow yourself to fall asleep." Testing starts immediately after instructions are given, and bedroom lights are turned off.
13. Each nap trial is ended if the patient does not fall asleep in 20 minutes. If sleep onset occurs, the trial is continued for an additional 15 minutes, regardless of the amount of intervening sleep or wake. Sleep onset is defined as the start of the first epoch scored as any stage of sleep.<sup>7</sup>
14. Stimulating activities such as the use of electronic devices and the use of cell phones should end at least 30 minutes before each nap trial. Vigorous physical activity and prolonged exposure to sunlight/bright artificial light should be avoided all day.
15. Between nap trials, the patient should be out of bed and not permitted to sleep.
16. A light breakfast at least 1 hour before the first trial and a light lunch immediately after the termination of the second nap trial are recommended.
17. Urine drug screening should be employed when indicated to ensure that the MSLT results are not confounded by inadvertent, intentional, or illicit medication or substance use.

**Data Acquisition and Reporting Procedures**

1. Patient demographics (name, DOB, test date, BMI, medical record number).
2. Names of referring clinician, sleep specialist, and sleep technologist.

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3. Documentation of medications used within 24 hours of and during the MSLT and changes to medications within last 2 weeks. If performed, the type of drug screening should be documented.
4. Documentation of available prestudy data including sleep diary, actigraphy, and PAP download.
5. Recording parameters including start time, end time, total sleep time, sleep latency, and REM sleep latency of each trial. Sleep latency is defined as the time from lights out until the start of the first epoch of any stage of sleep (an epoch of N1, N2, N3, or R). REM latency is defined as the time from the start of the first epoch of sleep until the start of the first epoch of stage R (REM sleep).
6. Mean sleep latency, number of SOREMPs during naps, and whether SOREMP occurred on the PSG. If no sleep occurs on a trial, 20 minutes is used for the sleep latency value and in the calculation of the mean sleep latency.
7. Deviations from ideal testing times and conditions (eg, caffeine, nicotine, napping, cell phone, fire alarms, or other stimulating activities) should be documented by the sleep technologist.
8. Interpretation of study findings with signature of board-certified sleep medicine specialist.

BMI = body mass index, DOB = date of birth, EEG = electroencephalogram, EKG = electrocardiogram, EMG = electromyogram, EOG = electro-oculogram, MSLT = Multiple Sleep Latency Test, PAP = positive airway pressure, PSG = polysomnogram, REM = rapid eye movement, SOREMP = sleep-onset rapid eye movement period.

MSLT. The MSLT should be interpreted by a board-certified sleep medicine specialist.

### Planning before the MSLT

**Sleep-wake scheduling before testing:** Documentation of sleep-wake schedules through sleep diaries with or without actigraphy for 2 weeks before testing is recommended to assure a consistent and sufficient amount of sleep, ie, ideally  $\geq 7$  hours per night leading up to the MSLT. The absolute minimum is 6 hours because some patients with narcolepsy experience fragmented sleep. Two weeks of data allow for monitoring of 2 weekends, a time wherein considerable variability may occur.

**Comorbid sleep disorders:** Patients with OSA or other sleep disorders may need an MSLT to evaluate for coexisting narcolepsy or another primary hypersomnia. Sleep-onset REM periods (SOREMPs) on the MSLT have been reported with severe untreated OSA, especially in patients with marked oxygen desaturation.<sup>8</sup> Accordingly, confirmation of positive airway pressure (PAP) adherence and effective treatment of OSA should precede the MSLT. A dose-response relationship between increasing PAP use and self-reported improvement in sleepiness has been reported, with an optimum response occurring with at least 6 hours of use per night.<sup>9</sup> Thus, current minimum adherence standards of  $\geq 4$  hours per night for 70% of the considered time<sup>10</sup> may not be sufficient for optimal resolution of sleepiness in some patients. No data have been found to inform treatment adherence standards for patients with central/complex sleep apnea or sleep-related hypoventilation who are undergoing an MSLT, but similar PAP adherence goals seem to be reasonable.

Although no studies have been found addressing the potential impact of PAP usage on sleep latency during the MSLT, the task force recommended that most patients accustomed to nighttime PAP/non-PAP therapies should use these interventions to reduce sleep disruption during the daytime nap trials. It has been reported that some patients with very mild OSA (apnea-hypopnea index  $< 10$  events/h) are intolerant to therapy.<sup>11</sup> For these patients, the clinician needs to balance the potential for disturbed sleep because of very mild OSA against the impact of disrupted sleep related to the OSA therapy in determining whether the therapy should be used during the MSLT. The test report should clearly state how OSA was managed during testing.

The timing of the MSLT is important. An individual's circadian phase could affect sleep latency and SOREMPs in shift workers

and patients with delayed sleep-phase disorder. Findings from the Wisconsin Sleep Cohort<sup>12</sup> showed a significant association between shift work (defined as stable night shift or rotating shifts) and MSLT results supporting a diagnosis of narcolepsy, ie, MSL  $\leq 8$  minutes and  $\geq 2$  SOREMPs, in patients who were unlikely to have narcolepsy. For patients with a delayed sleep phase, it is important to avoid ending polysomnography (PSG) prematurely, and especially to avoid disrupting or curtailing REM sleep. Accordingly, when evaluating shift workers and patients with a delayed sleep phase, clinicians should schedule the MSLT when the patient has a consistent sleep-wake schedule. In addition, the testing period should match the patient's typical wake period, which may require delaying the start of the MSLT to accommodate the later termination of the PSG for delayed or long sleepers. Consequently, assessment of the patient's sleep pattern and total sleep time for 2 weeks before the MSLT is important, and the use of actigraphy is suggested.<sup>13</sup> The use of the MSLT conducted at night for shift workers has not been systematically evaluated.

**Medications:** Medication use and discontinuation are particularly challenging issues because many agents can confound MSLT results and make interpretation of the test difficult.<sup>14–16</sup> For example, chronic use of certain medications suppresses REM sleep<sup>17</sup> and may inhibit SOREMPs on testing. Conversely, discontinuation of REM-sleep-suppressant medications immediately before the MSLT may result in REM sleep rebound, resulting in a false-positive MSLT.<sup>18</sup> The 2005 AASM practice parameter paper provided general guidance about which medication properties could interfere with an MSLT and recommended that stimulants, stimulant-type drugs, and REM-sleep-suppressing drugs be stopped 2 weeks before the test.<sup>3</sup> However, adherence to the 2005 recommendation is difficult, with 1 report indicating that only 5.9% of patients on REM-sleep-suppressant agents discontinued them before testing.<sup>19</sup> Frequently, patients experiencing excessive daytime sleepiness are being treated with stimulants or antidepressants for depression, anxiety, inattention, or fatigue. The task force recommends that the agents listed in [Table 1](#) (medications that can affect REM sleep and/or nonrapid eye movement sleep latency) be tapered before the MSLT to minimize medication and substance effects and that the patient be observed while off the agents for a sufficient time period before testing.<sup>20</sup> The exact duration of time that medications should be discontinued to avoid



medication or rebound effects on the MSLT has not been extensively studied, but a 2-week duration is considered likely sufficient in most patients. For medications or metabolites with longer half-lives ( $> 1$  day), a longer washout, potentially up to 6 weeks, may be necessary. In the case of medications with very short half-lives, consideration could be given to a washout of  $< 2$  weeks, particularly in patients in whom longer time off medication would negatively impact patient safety. Clinicians should avoid a washout so brief that the risk of REM sleep rebound is increased. Medication washout should ideally occur at a time that is least disruptive for a patient's safety, responsibilities, and/or productivity. In some patients, it may not be possible to discontinue a medication given concerns such as potentially suicidal depression or other adverse outcomes. In addition, a patient may communicate a strong preference to not discontinue medications. The task force suggests that clinicians and patients work in collaboration to develop a plan for managing medications to minimize disruption to the patient's life and avoid unintended consequences such as withdrawal. All medications taken by the patient 24 hours before the MSLT should be listed on the test report to aid in interpretation of results. If there is a negative result in a patient with a history strongly suggestive of narcolepsy, then the clinician should consider repeat testing or alternatively test orexin levels if cataplexy is present.

**Drugs and drug screening:** Consideration should be given to drug screening as part of the MSLT protocol, because several recreational and illicit drugs can affect both sleep and wake/alertness (ie, barbiturates, benzodiazepines, cannabinoids, cocaine, methadone, and opioids).<sup>21–23</sup> The available evidence suggests that up to 33% of adult patients undergoing MSLTs have a positive drug screen. Moreover, one study<sup>23</sup> found that 81% of the patients had not reported use of the detected substance.

The cost of drug screening can be significant depending on the type of test used. If there is concern about unreported substances or noncompliance with washout, drug screening 1–2 days before the test may be considered to facilitate rescheduling of the MSLT or if onsite specimen collection is not possible. Methods of drug screening vary from urine tests utilizing immunoassay technology to urine or blood testing using more advanced gas chromatography-mass spectroscopy techniques that can also test for prescription and over-the-counter products. After reviewing the literature, the task force concluded that drug screening may be indicated in adult patients depending on community and clinical circumstances.

Use of marijuana warrants specific attention because an increasing number of patients are using medical and recreational marijuana as a result of legalization in several states. There is a limited but evolving body of literature addressing the impact of marijuana on MSLT outcomes.<sup>24–28</sup> Both acute and chronic tetrahydrocannabinol use have been reported to induce sleep.<sup>21</sup> One of the most pertinent findings regarding marijuana use is that recent discontinuation can result in REM sleep rebound.<sup>29</sup> Thus, similar to other medications that can affect sleep-wake and MSLT results, when a washout period is not possible, a stable dose and consistent use of marijuana for at least 2 weeks before the MSLT is recommended. Clinicians should be aware that tetrahydrocannabinol has a long half-life, so a 2-week washout may not be sufficient for a negative drug screen.

**Caffeine:** Caffeine use before testing is challenging because of the diversity of products, patterns of consumption, and varying degree

of tolerance/withdrawal symptoms. In addition, a recent study showed that in regular caffeine users, consumption of caffeine 13.5 hours before bedtime delayed both non-REM sleep and REM sleep latencies.<sup>30</sup> The observed caffeine effect was not detectable at 44.5 hours after caffeine withdrawal compared to placebo. The results suggest that a specific time frame for abstinence is needed to eliminate caffeine effects. One approach is to request that all patients abstain on the days of the PSG and MSLT, but clinicians should determine whether certain patients should be tapered off caffeine over a longer period preceding testing.

### General testing and data acquisition

**PSG before MSLT:** Facility-based PSG is necessary on the night before the MSLT to assess sleep architecture and confirm adequate nocturnal sleep.<sup>31</sup> Adequate sleep duration must be obtained during the PSG preceding the MSLT to prevent potential confounding because of insufficient sleep. Overall, there has been consensus that patients need to obtain a minimum of 6 hours of total sleep time during at least 7 hours of total recording time to address the specific needs of patients with suspected narcolepsy.<sup>32</sup> The PSG duration may need to be extended to avoid insufficient sleep confounding the results.<sup>4</sup> Split-night PSG should be avoided because it does not represent a full night of sleep uninterrupted by respiratory events and/or PAP therapy adjustments. Furthermore, PSG is necessary to determine whether a SOREMP occurred within 15 minutes of nighttime sleep onset, an ICSD-3 diagnostic criterion for narcolepsy.<sup>4</sup> The task force recommends that the same electroencephalogram montage be used for PSG and the MSLT (F3-M2 or F4-M1, C3-M2 or C4-M1, O1-M2 or O2-M1 derivations) so that there is no need to change the electrode placement in the morning. Substituting a home sleep apnea test on the night before the MSLT is not acceptable because of limitations regarding sleep data.<sup>31</sup>

**Environmental factors:** Even minimally stimulating activities, eg, 5 minutes of walking just before a nap trial<sup>33</sup> can cause physiological arousal and significantly increase sleep latency on an MSLT.<sup>34–40</sup> Therefore, the task force suggests that stimulating activities, including the use of all electronic devices, should be stopped 30 minutes before the start of each nap. Room temperature should be set to patient preference. The patient's clothing should be nonrestricting. During nap trials, window shades should be closed and ideally blackout shades should be used to prevent light intrusion. The bed should be comfortable. Patients should be out of bed between nap trials because lying in bed watching television within 15 minutes of a nap trial may reduce sleep latencies and confound the interpretation of the results.<sup>33</sup>

**Performance of nap trials:** The consistent performance of bio-calibrations provides time for the stabilization of arousal levels before nap trials. The sleep technologists should ensure that the nap trials start on time. A minimum of 4 naps is required for the MSLT because the ICSD-3 diagnostic criteria are based on a minimum of 4 naps,<sup>5</sup> and fewer naps diminish the reliability of the sleep latency measure.<sup>19,41</sup> In weighing benefits and potential harms,<sup>42</sup> the TF determined that a fifth nap trial is preferred.

Each nap trial should be terminated 15 minutes after an epoch of sleep or after 20 minutes if no epoch of sleep is identified.

Therefore, the total duration of each nap trial can vary from 20–35 minutes.

## PROTOCOLS FOR MWT

The protocol for the MWT is presented in **Box 3** and **Box 4**.

### Considerations for the MWT

The objective of the MWT is to measure the patient's alertness and/or ability to stay awake. The MWT may be performed to (1) determine the effect of medications, substances, or other interventions

compared to pretreatment or normal controls; or (2) determine the patient's nonpharmacologic state compared to normal controls. Several factors concerning patient preparation and test performance need to be considered to acquire reliable data for the MWT. These considerations are discussed in detail herein and are intended to provide sleep testing providers with additional guidance in conducting the MWT. The MWT should be ordered and interpreted by a board-certified sleep medicine physician.

### Planning before the MWT

**Sleep-wake schedule before testing:** Documentation of sleep-wake schedules and adequate sleep time, although not mandatory, may be helpful in interpreting the findings. The use of sleep

#### Box 3—MWT clinical guidance and patient preparation before testing.

1. In preparation, the clinician and the patient should define goals for adequate sleep with regard to timing and duration. Adequate sleep should be documented by sleep diary and, whenever possible, actigraphy for 2 weeks before testing.
2. The MWT should be conducted when a patient is clinically stable and when treatments of any known sleep disorders are well-established and effective.
3. In patients with sleep-disordered breathing who are being evaluated for the effectiveness of therapy, the clinician should ensure effectiveness (efficacy and adherence) based on a review of downloaded data or self-reported use for non-PAP before testing. If adequate effectiveness is suboptimal, then the clinician should determine if the anticipated impact on the test results warrants rescheduling. The patient should use PAP/non-PAP therapy on the night before the MWT.
4. The clinician should develop a plan regarding the use of prescription medications, OTC agents, herbal remedies, and other substances. If the patient is chronically taking medications with alerting or sedating properties, then they should be continued at a stable dose. Changes in medications should be avoided for 2 weeks before testing. The patient should be instructed to consult with the clinician before starting a prescription or OTC medication before the test.
5. The ordering clinician in consultation with the patient should clarify acceptable caffeine consumption before the MWT.

MWT = Maintenance of Wakefulness Test, OTC = over the counter, PAP = positive airway pressure.

#### Box 4—MWT general testing, data acquisition, and data reporting procedures.

##### General Testing Procedures

1. Relevant clinical data such as preceding sleep schedules, PAP adherence, or other therapies should be available to the interpreting clinician. The MWT should be performed after the patient's major sleep period. Performance of a PSG before the MWT is at the discretion of the sleep clinician.
2. The patient's clothing should be comfortable, be appropriate to the environment, and not interfere with the performance of tests. If a PSG is performed, then a change in clothing is not required between the PSG and the MWT.
3. The patient should abstain from alcohol, marijuana, and other sedating substances on the day of the test.
4. Patients on PAP/non-PAP therapies for sleep-disordered breathing should use them the night before (but not during) the MWT. If a PSG is performed, then the PAP settings and mask interface should match those used at home.
5. The recording montage for the MWT should, at a minimum, include 3 EEG recording leads with 1 each for frontal (F3-M1 or F4-M2), central (C3-M2 or C4-M1), and occipital (O1-M2 or O2-M1) derivations, left and right eye EOGs, mental/submental EMG, and EKG.
6. Audiovisual recordings must be made during the wake trials and be accessible to interpreting sleep specialists. The patient must be audiovisually monitored throughout the day, but retention of recordings made between trials is discretionary.
7. The MWT should consist of four 40-minute wake trials. The initial trial should begin 1.5–3 hours after termination of the preceding night's sleep at home, and a subsequent trial should begin 2 hours after the start of the prior trial.
8. Before each wake trial, the patient should be offered the use of the restroom and queried regarding other requirements for comfort.
9. Sleep rooms should be dimly lit, quiet, and at a comfortable temperature during testing. The light source should deliver an illuminance of 0.1–0.13 lux at the corneal level (such as a 7.5-watt nightlight) placed 12 inches off the floor and 3 feet lateral to the patient's head. The patient should be given sufficient time to acclimate to the recording room before the start of the first trial.
10. The patient should be seated in a bed or reclining chair with the back and head comfortably supported. This should be the same for all wake trials.
11. Patient bio-calibrations should be conducted before starting each wake trial. Standard instructions include: (1) "sit quietly with your eyes open for 30 seconds"; (2) "close both eyes for 30 seconds"; (3) "without moving your head, look to the right, then left, then right, then left, right and then left"; (4) "blink eyes slowly for 5 times"; and (5) "clench or grit your teeth tightly together." Before the trials, patients should be instructed to refrain from activities and vocalizations that promote wakefulness such as fidgeting or singing.
12. At the start of each wake trial, the patient should be instructed as follows: "Please sit still and remain awake for as long as possible. Look directly ahead of you, and do not look directly at the light." Testing starts immediately after instructions are given, and bedroom lights are turned off.

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13. Each wake trial is ended once the patient has 3 consecutive epochs of stage N1 sleep or 1 epoch of any other sleep stage or after 40 minutes.
14. Stimulating activities such as consuming nicotine and the use of electronic devices and cell phones should end at least 30 minutes before each wake trial. Vigorous physical activity and prolonged exposures to sunlight/bright artificial light should be avoided all day.
15. Between wake trials, the patient should be out of bed and not permitted to sleep.
16. A light breakfast at least 1 hour before the first wake trial and a light lunch immediately after the termination of the second wake trial are recommended.
17. Urine drug screening should be employed when indicated to ensure that the MWT results are not confounded by inadvertent, intentional, or illicit medication or substance use.

#### Data Acquisition and Reporting

1. Patient demographics (name, DOB, test date, BMI, medical record number).
2. Names of referring clinician, sleep specialist, and sleep technologist.
3. Documentation of medications used within 24 hours of and during the MWT and any changes to medications within last 2 weeks. If performed, the type of drug screening should be documented.
4. Documentation of available prestudy data including sleep diary, actigraphy, and PAP download.
5. Recording parameters including start time, end time, total sleep time, and sleep latency of each wake trial. Sleep latency is defined as the time from lights out until the start of the first epoch of any stage of sleep (an epoch of N1, N2, N3, or R).
6. Mean sleep latency averaged over the 4 wake trials. If no sleep occurs on a trial, then 40 minutes is used as the sleep latency and in the calculation of the mean sleep latency.
7. Deviations from ideal testing times and conditions (eg, nicotine, caffeine, napping, cell phone, fire alarms, or other stimulating activities), should be documented by the sleep technologist.
8. Interpretation of study findings with signature of board-certified sleep medicine physician.

BMI = body mass index, DOB = date of birth, EEG = electroencephalogram, EKG = electrocardiogram, EMG = electromyogram, EOG = electro-oculogram, MWT = Maintenance of Wakefulness Test, PAP = positive airway pressure, PSG = polysomnogram.

diaries and/or actigraphy is recommended for 2 weeks before testing. Most patients having an MWT are motivated to stay awake, so insufficient sleep is less of a concern than substance use. In addition, the MWT may be conducted to evaluate alertness following the patient's typical sleep patterns.

**Comorbid sleep disorders:** The ordering clinician and patient should establish goals for adequate treatment of coexisting disorders before the MWT. Patients with OSA on PAP or non-PAP therapy should be advised to use their therapy consistently and adequately at night in the weeks before the MWT. The Apnea Positive Pressure Long-Term Efficacy Study showed that an increase in MSL from baseline to 6-month follow-up correlated with mean nightly PAP use of > 4 hours.<sup>9</sup> Similar to the MSLT, patients on PAP therapy who are preparing for the MWT should try to optimize PAP usage. Sleep apnea therapies should not be used during the wake trials because the patient is instructed to stay awake. There have been no studies found concerning the impact of treatment for central or complex sleep apnea on the MWT.

Although the use of the MWT during the night for shift workers has not been systematically evaluated, determining circadian rhythm patterns and total sleep time before the MWT is important because it could affect the MWT results. Therefore, it is recommended that patients have a stable sleep schedule before testing. Stimulating activities that could promote wakefulness should also be avoided before MWT trials.

**Medications and stimulants:** If the patient is on a pharmacologic or other intervention for a sleep-wake disorder, then the intervention should be consistently used with a stable treatment regimen. Treatment adjustments should be avoided before the study. In addition, patients should remain on their usual, chronic medications so that the MWT data reflect their stable condition and potential withdrawal issues are avoided. The use of medications should be documented, including the use of caffeine, alcohol, and marijuana.

If the MWT is used to provide information about the effectiveness of treatment, then the conditions of the test would allow for the use of prescribed alerting agents or typical caffeine use during the day.

**Drugs and drug screening:** The clinician must decide whether drug screening is necessary. A drug screen, although not required, may identify unreported medication or drug use. In a study by Annis et al,<sup>22</sup> 6 out of 26 patients (16%) undergoing an MWT had a positive drug screen for either an amphetamine, cannabis, or benzodiazepine. A variety of reasons motivated patients for their unreported drug use. If a drug screen is performed, then the results should be clearly documented in the test report.

#### General testing and data acquisition

**PSG before the MWT:** The need to perform a PSG on the night before the MWT is controversial. A PSG before the MWT is left to the discretion of the clinician. Unlike with the MSLT, the addition of a PSG showing normal and adequate sleep does not always inform the results of the MWT or impact its interpretation. The MWT provides an objective indicator of a person's ability to maintain wakefulness in a controlled setting. Unlike the MSLT, the MWT is not a diagnostic test. It is more commonly ordered for patients who deny daytime sleepiness and are motivated to stay awake throughout the day. Adequate sleep quality and duration in the night preceding testing is essential. Rescheduling the test should be considered if a patient reports inadequate sleep on the night preceding the scheduled MWT.

There are circumstances in which a PSG before an MWT may be useful, such as when there is suspicion of a sleep disorder and a PSG has not previously been performed. Previous work has indicated that the amount of sleep during the prior week, the number of oxygen desaturations > 4% during a PSG, and recent medication adjustments impact objective measures of sleep latency.<sup>10</sup> A PSG may also be warranted if there is potential secondary gain (eg,

prescription for stimulants) to patients if they are found to be sleepy on the day of the test.<sup>4</sup> For example, patients motivated to manifest sleepiness may use various methods such as sleep deprivation. A PSG before the MWT can control for acute sleep deprivation. In addition, overnight testing can assist in monitoring acute use of stimulants such as caffeine. Finally, overnight testing avoids the promotion of alertness during the first wake trial that may occur when a patient drives to the testing center, is exposed to bright outdoor light exposure, and has sensor application procedures in the morning. Despite the circumstances in which a prior PSG may be beneficial, it was the consensus of the task force that performing a PSG before the MWT is optional and at the discretion of the clinician.

**Environmental factors:** Patients should stop all stimulating activities including the use of electronic devices 30 minutes before each wake trial to decrease the impact of such activities on the test results. The patient should sit in a chair or on the bed during the wake trial. The 2005 AASM protocol suggests that a patient be seated on a bed to prevent injury.<sup>43</sup> The task force recognized that utilizing a bed does not reflect a typical occupational or safety-sensitive setting, and survey data indicated that patients are sometimes allowed to sit in a reclining chair. The task force

recognized the potential impact of sitting in a chair vs sitting upright in bed on the patient’s physical comfort and positioning during tasks requiring alertness. Because the task force found no evidence concerning the impact of sitting in a bed vs a chair and because sitting in a chair during the day is a more typical activity, it was the consensus of the task force that either option could be used but must be consistent for all the wake trials.

**Recording montage:** The task force recommended that the same recording montage be used for the MWT as for the MSLT.

**Performance of wake trials:** The task force found limited data about variations in the number and duration of wake trials. The 2005 AASM protocol<sup>43</sup> recommended four 40-minute wake trials. Since the publication of the protocol, no alternative procedures for the MWT have emerged. One study evaluated the use of an additional fifth wake trial to prevent the long latency because of the “last nap effect” from impacting the fourth trial and spuriously increasing the MSL of the 4 trials. This approach resulted in a longer testing day and has not been embraced in clinical practice.<sup>44</sup> However, extending the testing day to include a fifth wake trial may still fail to capture all the sleep onsets observed in some patients with impaired alertness.<sup>10</sup>

Table 1—Medications that may interfere with sleep architecture.<sup>44</sup>

Drug Class	Example Agents <sup>44</sup>
Acetylcholine modulators	Donepezil <sup>45</sup>
Adenosine modulators	Theophylline, <sup>46</sup> theobromine, caffeine
Alpha-2 delta ligands	Gabapentin
Antidepressants	
SSRIs <sup>47</sup>	Fluoxetine <sup>20*</sup> , escitalopram, <sup>48</sup> sertraline, paroxetine
SNRIs	Venlafaxine, duloxetine <sup>49</sup>
Bupropion	Bupropion <sup>50</sup>
Tricyclic antidepressants	Nortriptyline, amitriptyline <sup>48</sup>
MAOIs	Phenelzine <sup>51</sup>
Antihistamine, sedating	Diphenhydramine, doxylamine
Antipsychotic agents	Quetiapine <sup>52</sup>
Antihypertensives	Prazosin <sup>53</sup>
Benzodiazepines/NBRAs	Flurazepam*, clonazepam, lorazepam, zolpidem, eszopiclone, zaleplon
Dopamine agonists	Pramipexole, rotigotine, ropinirole <sup>54</sup>
Lithium	Lithium
Melatonin agonists	Ramelteon, tasimelteon
Opioid agonists	Morphine, hydrocodone, methadone, <sup>55</sup> fentanyl <sup>56</sup>
Orexin/hypocretin antagonists	Suvorexant <sup>57</sup>
Sodium oxybate	Sodium oxybate <sup>58</sup>
Steroids	Prednisone <sup>59</sup>
Stimulants	Methylphenidates, amphetamines
Wake-promoting agents	Armodafinil, modafinil, pitolisant, solriamfetol
Marijuana	Tetrahydrocannabinol <sup>60*</sup>

Table includes commonly encountered medications or those requiring a prolonged washout period, but it is not an exhaustive list. A 2-week washout is generally recommended. \*Medication agents with long half-lives and longer washout (up to 6 weeks) may be needed. CBG = cannabigerol, MAOIs = monoamine oxidase inhibitors, NBRAs = nonbenzodiazepine receptor agonists, SNRIs = serotonin noradrenergic reuptake inhibitors, SSRIs = selective serotonin reuptake agonists.



**Interpretation considerations:** Abnormal cutoffs for the MSL have not been determined for the MWT. The modal MSL on the MWT is 40 minutes, indicating a ceiling effect.<sup>3</sup> MSL values are compared to normative values or to previous values from the same individual depending on the purpose of the test. The published literature suggests that mean latency and deviation for normal control patients on the MWT is  $30.4 \pm 11.20$  minutes. Depending on the clinical circumstances, an MSL above the mean may be more desirable whereas with other patients, values in the normal range may be acceptable. Within-patient comparisons can help determine the effect of medications or other interventions on alertness.

## DISCUSSION

The MSLT and MWT are affected by many physiological, psychological, and operational variables that providers need to be aware of when ordering, conducting, and interpreting the tests. Several protocol changes were adopted in this document. A technical change to include the frontal electrodes was made for consistency with the current scoring recommendations for sleep staging. These changes are consistent with the current recommendations for PSG recordings in *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*.<sup>7</sup> In addition, a procedural change specifies the termination of stimulating activity 30 minutes before naps/trials, including the use of all electronic devices for both the MSLT and the MWT. This factor eliminates the prior 15- and 30-minute distinction for different activities, which could contribute to more stable patient arousal levels at the start of each trial. Most notably, there is additional guidance concerning the amount of sleep leading up to testing, sufficient treatment of OSA, and shared patient-clinician decision-making concerning the use of medications and caffeine. Patients should obtain at least 6 hours of sleep, preferably more than 7 hours, before testing with concomitant use of OSA treatment, if applicable. PAP and non-PAP treatments should also be used during each nap trial for the MSLT.

Adherence to the testing protocol and the use of standardized reporting will increase the value of the MSLT and MWT results. In general, a diagnosis of hypersomnia should be made with extreme care and with as much clinical information as possible. The diagnosis can affect an individual's job or ability to pursue safety-sensitive activities like driving. Neither the MSLT nor MWT should be the sole criterion for determination of excessive sleepiness, certification of a diagnosis, or proof of response to treatment. Such conclusions should be based on interpretation of the MSLT or MWT results in combination with the individual patient history or other relevant data.

## Future directions

Future research should address the effect of protocol modifications on sleep latency and operational characteristics of the tests, along with the impact of various medications, treatments for OSA, and sleep-wake cycles on test results. Additional large normative data and validation studies are also needed for both tests to help establish diagnostic criteria. Studies examining the impact of factors such as shift work, medications, hormonal cycles, and recreational substances on each test are needed. One study examined the use of a fixed

duration of nap trials on MSLT findings, but further research is needed on the impact of changes in nap duration on SOREMPs.<sup>61</sup> Data show that MSLT findings vary by age, suggesting that age-specific diagnostic criteria may need to be developed, particularly for children and older adults.<sup>19</sup> Research on MWT results and their relationship to driving and workplace safety are needed and could potentially provide diagnostic and treatment cutoffs. Ultimately, more time-efficient and cost-effective tests are needed to assess sleepiness and wakefulness. Especially valuable would be the development of fast and reliable field tests for sleepiness and alertness.

## ABBREVIATIONS

AASM, American Academy of Sleep Medicine  
MSL, mean sleep latency  
MSLT, Multiple Sleep Latency Test  
MWT, Maintenance of Wakefulness Test  
OSA, obstructive sleep apnea  
PAP, positive airway pressure  
PSG, polysomnography  
REM, rapid eye movement  
SOREMP, sleep-onset rapid eye movement period

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